

## REMARKS

Claims 1-13, 27, 28, 30, 32-34, 51 and 52 are pending. Claim 6 is cancelled without prejudice.

Claims 1, 7 and 51 are amended herein. The language of the amendments to claims 1 and 51 is supported in the specification at claim 6 as originally filed, and in the specification at, for example, page 9, lines 7-15. Claim 7 is amended merely to change its dependency from cancelled claim 6 to amended claim 1. The amendments add no new matter.

### Priority:

The Office Action states that an application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet. The amendment to the specification made herein is made to comply with this formality. Applicant notes that the filing papers, including the New Utility Application Transmittal included the claim to the priority under §119(e) of U.S. provisional application 60/179,283, filed January 31, 2000. The amendment adds no new matter.

### Rejections under 35 U.S.C. §102(b):

Claims 1, 3, 4, 27, 28 and 32 are rejected under 35 U.S.C. §102(b) over Blau et al. (WO 98/44350). The Office Action states that “Blau et al. disclose methods for detecting protein-protein interactions,” and that “the phosphorylation of one of the binding partners endows it to associate with another of the binding partners.” The Office Action also states that the reference teaches that “the interactions can be detected by using reporter subunits (tag) which produce a chromogenic, fluorescent or luminescent signals” and that “the reporter subunits may comprise fluorophores which are capable of detectable resonance energy transfer when they are closely associated.” Finally, the Office Action states that the reference discloses “that the methods can be used to study agonists and antagonists of a binding interaction.” The Office Action thus concludes that the claims are anticipated. Applicant respectfully disagrees.

Applicant submits that Blau et al. does not teach a method for monitoring the activity of one or more enzymes comprising a step of detecting binding or dissociation, wherein the step

further comprises adding one or more detector molecules comprising a first region that associates with the one or more tagged binding partner polypeptides and a second region comprising one or more reporter molecules, as required by claim 1 as amended. Because Blau et al. does not teach adding one or more detector molecules comprising a first region that associates with the one or more tagged binding partner polypeptides and a second region comprising one or more reporter molecules, as required by claim 1 as amended, Applicant submits that the reference cannot anticipate claim 1 as amended or claims 3, 4, 27, 28 and 32 that depend from it. Applicant respectfully requests withdrawal of this rejection.

Claims 1-4, 28 and 32-34 are rejected under 35 U.S.C. §102(e) over Heroux et al. (S.S. 6,312,896). The Office Action states that “Heroux et al. disclose methods for measuring the activity of enzymes.” The Office Action states that the reference “discloses mixing two substrates and an enzyme which catalyzes a change in the substrate molecule (for example phosphorylation of a protein) that induces the substrate to bind to a second molecule.” The Office Action further states that “Heroux et al. disclose that the substrates can be labeled (tagged) with ECL labels,” and that the reference discloses “that the invention can be used to assay an enzyme inhibitor and/or to measure the inhibitory ability of [a] test compound.” The Office Action thus concludes that the claims are anticipated. Applicant respectfully disagrees.

Applicant submits that Heroux et al. does not teach a method for monitoring the activity of one or more enzymes comprising a step of detecting binding or dissociation, wherein the step further comprises adding one or more detector molecules comprising a first region that associates with the one or more tagged binding partner polypeptides and a second region comprising one or more reporter molecules, as required by claim 1 as amended. Because Heroux et al. does not teach adding one or more detector molecules comprising a first region that associates with the one or more tagged binding partner polypeptides and a second region comprising one or more reporter molecules, as required by claim 1 as amended, Applicant submits that the reference cannot anticipate claim 1 as amended or claims 2-4, 28 and 32-34 that depend from it. Applicant respectfully requests withdrawal of this rejection.

Rejections under 35 U.S.C. §103:

Claims 5-13, 30 and 51 are rejected under 35 U.S.C. §103(a) as being obvious over Blau et al. in view of Colyer et al. (U.S. 6,465,199). The Office Action states that the teachings of Blau et al. “differ from the instant invention in failing to teach the polypeptides comprise one or more radioactive molecules” and “fail to teach the detection of the amount of binding or dissociation in the presence of the candidate modulator that is lesser or greater as compared to the amount of binding or dissociation in the absence of the candidate modulator.” The Office Action states that the Blau et al. reference also fails to teach “monitoring the rate of diffusion of the fluorescent molecule.” The Office Action cites Colyer et al. as providing the missing aspects of the claims, and states that “it would have been obvious to one of ordinary skill in the art to incorporate labels and controls as taught by Colyer et al. into the method of Blau et al. because Colyer et al. shows that the use of such labels, controls and FCS provide for efficient means of monitoring post-translational modification of a protein and provides for a technique in which the addition/removal of a modifying group can be monitored continuously during real time to provide a dynamic assay system that also has the ability to resolve spatial information. Applicant respectfully disagrees.

Claim 52 is rejected under §103(a) as obvious over Blau et al. in view of Colyer et al. in further view of Heroux et al. For the reasons explained below, Applicant respectfully disagrees.

First, Applicant submits that Colyer et al. does not teach a detecting step that comprises adding one or more detector molecules comprising a first region that associates with the one or more tagged binding partner polypeptides and a second region comprising one or more reporter molecules, as required by claim 1 and claim 51 as amended. As discussed above, neither Blau et al. nor Heroux et al. teaches this limitation. Because none of Blau et al., Heroux et al. and Colyer et al. teach such a limitation, Applicant submits that claims 5, 7-13 and 30 which ultimately depend from claim 1 as amended, and claim 51 as amended cannot be obvious over any combination of these references (the rejection is moot as to claim 6, which is cancelled herein). Similarly, claim 52, which depends from amended claim 51 cannot be obvious over any combination of these references.

Second, Applicant submits that Colyer et al. is not prior art over the present application under 35 U.S.C. §103(c). Specifically, §103(c) precludes the use of subject matter, 1) developed by another person, which 2) qualifies as prior art only under §102(e), (f) or (g), in an obviousness rejection where 3) such subject matter and the claimed subject matter were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. These elements of §103(c) are met by the Colyer et al. patent as detailed below.

1) The inventive entities of the present application and the '199 patent are different - the inventive entity of the present application is Roger C. Craig, while the inventive entity of the '199 patent is Roger C. Craig and John Colyer. Therefore, the '199 patent is "by another."

2) Applicant submits that the '199 patent is a U.S. patent that is potentially prior art only under §102(e), having issued after filing of the present application from an application filed before the filing date of the present application. The present application has an effective filing date of January 31, 2000 (based on the filing of provisional application 60/179,283), and the Colyer et al. patent issued from an application filed February 26, 1999.

3) Applicant submits that at the time the present invention was made, the application that matured into the '199 patent and the present invention were subject to an obligation of assignment to the same company, Fluorescence Limited, as evidenced by the following assignments. (Fluorescence Limited was subsequently acquired by Cyclacel Limited which is listed as the assignee on the face of the '199 patent.)

Enclosed are: i) a copy of the Notice of Recordation of the assignment of the provisional application 60/179,283 from inventor Roger K. Craig to Fluorescence, Ltd., recorded at Reel 010767, Frame 0726, noting the date of execution of the assignment as February 8, 2000 – the assignment covers any and all other applications filed on the invention or improvements, and thus covers the present utility application; and ii) a copy of the assignment of the application that matured into the Colyer et al. '199 patent from Fluorescence Limited to Cyclacel Limited, executed on October 27, 2000 and recorded at Reel 011792, Frame 0764. Applicant submits that the assignment records document the common ownership (by Fluorescence) of the two

inventions at the time the subject invention was made, as well as the obligation to assign both inventions to Fluorescence at the time the invention was made.

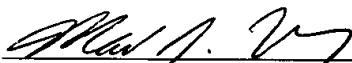
In view of the above, Applicant submits that Colyer et al. is not prior art over the present application. Thus, Colyer et al. cannot be combined with Blau et al. or Heroux et al in an obviousness rejection. In view of this, Applicant submits that claims 5, 7-13, 30, 51 and 52 are not obvious over the cited art. Applicant respectfully requests the withdrawal of the §103 rejection.

In view of the above, Applicant submits that all issues raised in the Office Action have been addressed herein. Applicant respectfully requests reconsideration of the claims.

Respectfully submitted,

*Mark J. Fitzgerald*  
*Reg. No. 45,928 for*  
*Kathleen Williams*

Date: June 27, 2003



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UNITED STATES DEPARTMENT OF COMMERCE  
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JULY 11, 2000

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BANNER & WITCOFF, LTD.  
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BOSTON, MA 02109



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UNITED STATES PATENT AND TRADEMARK OFFICE  
NOTICE OF RECORDATION OF ASSIGNMENT DOCUMENT

THE ENCLOSED DOCUMENT HAS BEEN RECORDED BY THE ASSIGNMENT DIVISION OF THE U.S. PATENT AND TRADEMARK OFFICE. A COMPLETE MICROFILM COPY IS AVAILABLE AT THE ASSIGNMENT SEARCH ROOM ON THE REEL AND FRAME NUMBER REFERENCED BELOW.

PLEASE REVIEW ALL INFORMATION CONTAINED ON THIS NOTICE. THE INFORMATION CONTAINED ON THIS RECORDATION NOTICE REFLECTS THE DATA PRESENT IN THE PATENT AND TRADEMARK ASSIGNMENT SYSTEM. IF YOU SHOULD FIND ANY ERRORS OR HAVE QUESTIONS CONCERNING THIS NOTICE, YOU MAY CONTACT THE EMPLOYEE WHOSE NAME APPEARS ON THIS NOTICE AT 703-308-9723. PLEASE SEND REQUEST FOR CORRECTION TO: U.S. PATENT AND TRADEMARK OFFICE, ASSIGNMENT DIVISION, BOX ASSIGNMENTS, CG-4, 1213 JEFFERSON DAVIS HWY, SUITE 320, WASHINGTON, D.C. 20231.

RECORDATION DATE: 04/19/2000

REEL/FRAME: 010767/0726  
NUMBER OF PAGES: 3

BRIEF: ASSIGNMENT OF ASSIGNOR'S INTEREST (SEE DOCUMENT FOR DETAILS).

ASSIGNOR:  
CRAIG, ROGER K.

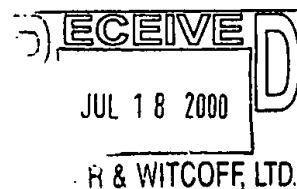
DOC DATE: 02/08/2000

ASSIGNEE:  
FLUORESCIENCE, LTD.  
P.O. BOX 439  
LEEDS, ENGLAND

SERIAL NUMBER: 60179283  
PATENT NUMBER:

FILING DATE: 01/31/2000  
ISSUE DATE:

DOROTHY RILEY, PARALEGAL  
ASSIGNMENT DIVISION  
OFFICE OF PUBLIC RECORDS



05-11-2000

FORM PTO-1595

RECO

U.S. DEPARTMENT OF COMMERCE  
PATENT AND TRADEMARK OFFICETo the Honorable Commissioner of Patents :  
Please record the attached original document or copy thereof.

101353230

1. Name of conveying party(ies):

4.19.00

Roger K. Craig

2. Name and address of receiving party(ies):

Name:

Fluorescence, Ltd.

Internal Address:

Street Address:

P.O. Box 439

City: Leeds

Country: England

Postal Code ZIP:

Additional name(s) of conveying party(ies) attached?

YES ☒ NO ☒

3. Nature of conveyance:

☒ Assignment ☐ Merger☐ Security Agreement ☐ Change of Name☐ Other

Additional name(s) &amp; address(es) attached?

☐ YES ☒ NO

Execution Date: February 8, 2000

4. Application number(s) or patent number(s):

If this document is being filed together with a new application, the execution date of the application is:

A. Patent Application No.(s):

60/179,283

B. Patent No.(s):

Additional application or patent numbers attached? YES ☐ NO ☒

5. Name and address of party to whom correspondence concerning document should be mailed:

Name: Kathleen M. Williams, Esq.  
Banner & Witcoff, Ltd.

Address: 28 State Street, 28th Floor

City: Boston

State: MA. Zip: 02109

6. Total number of applications and patents involved: 1

7. Total Fee (37 CFR 3.41) \$ 40.00

☒ Enclosed ☐ Authorized to charge Deposit Account 19-0733

8. Should any fee adjustment be necessary to effect proper recordation, please debit or credit our Deposit Account No. 19-0733, as necessary.

05/11/2000 JSHABAZZ 00000260 60179283

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01 Fee: 581

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9. Statement and signature.

To the best of my knowledge and belief, the foregoing information is true and correct and any attached copy is a true copy of the original document.

Kathleen M. Williams, Reg. No. 34,380

Name of Person Signing

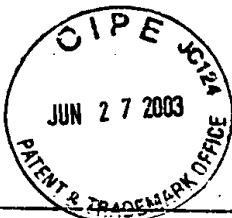
Signature

Date

Atty. Docket No.: 4256/85181

Total number of pages including cover sheet, attachments and document: 3

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05-16-2001

FORM PTO-1595



ER SHEET

U.S. Department of Commerce

5-9-01

101719294

To the Honorable Commissioner of Patents and Trademarks: Please record the attached original documents or copy thereof.

## 1. Name and address of conveying party(ies):

Name: Fluorescence LimitedStreet Address: 55 Colmore RowCity: Birmingham, West Midlands England B3 2AS

State: \_\_\_\_\_ ZIP: \_\_\_\_\_

Additional name(s) of conveying party(ies) attached? ☐ Yes ☒ No

## 2. Name and address of receiving party(ies):

Name: Cyclacel Limited

Internal Address: \_\_\_\_\_

Internal Address: \_\_\_\_\_

Street Address: 21 St. James SquareCity: London SW1Y 4RB England

State: \_\_\_\_\_ ZIP: \_\_\_\_\_

Additional name(s) and address(es) attached? ☐ Yes ☒ No

## 3. Nature of Conveyance:

☒ Assignment☐

Merger

☐ Security Agreement☐

Change of Name

☐ Other \_\_\_\_\_Execution Date: October 27, 2000

## 4. Application number(s) or registration numbers:

If being submitted with New Application, execution date of application is:

A. Patent Application No.(s) 09/146,549

B. Patent No.(s) \_\_\_\_\_

Additional numbers attached? ☒ Yes ☐ No

## 5. Name and address of party to whom correspondence concerning document should be mailed:

Name: Kathleen M. WilliamsInternal Address: Palmer & Dodge LLPStreet Address: One Beacon StreetCity: Boston State: MA ZIP: 021086. Total number of application and patents involved: 77. Total fee (37 CFR 3.41) ..... \$ 280.00☒ Enclosed☐ Authorized to charge deficiencies to deposit account8. Deposit account number: 16-0085 Ref. 10069/00001

(Attach duplicate copy of this page if paying by deposit account)

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## 9. Statement and signature.

To the best of my knowledge and belief, the foregoing information is true and correct and any attached copy is a true copy of the original document.

Kathleen M. Williams

Name of Person Signing

Signature

Date

5/9/01

Total number of pages comprising cover sheet attachment and document: 8Mail documents to be recorded with required cover sheet information to:  
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Washington, D.C. 20231

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PATENT  
REEL: 011792 FRAME: 0761



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Express Mail Label No.: EL591998485US

Additional Application Numbers:

09/259,474

09/259,658

09/259,981

09/259,478

09/258,452

09/259,159

PATENT  
REEL: 011792 FRAME: 0762

215  
3009

Dated 27 October 2000

**FLUORESCIENCE LIMITED**

and

**CYCLACEL LIMITED**

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**PATENT ASSIGNMENT**

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**K**  
Solicitors  
107-111 Fleet Street  
London  
EC4A 2AB

**PATENT**  
**REEL: 011792 FRAME: 0763**

THIS AGREEMENT is made the 27<sup>th</sup> day of October

2000

BETWEEN

(1) **FLUORESCIENCE LIMITED**, a company registered in England and Wales (registered number 03378741) whose registered office is at 55 Colmore Row, Birmingham, West Midlands, B3 2AS (the "Assignor"); and

(2) **CYCLACEL LIMITED**, a company registered in England and Wales (registered number 3237549) whose registered office is 12 St. James Square, London SW1Y 4RB (the "Assignee").

WHEREAS:

- (A) The Assignor is the registered proprietor or the Applicant for registration of the patents and applications listed in the Schedule to this Agreement;
- (B) Pursuant to a Business Purchase Agreement of even date ("BPA"), the Assignor has agreed to assign to the Assignee the said registered patents and applications together with any other patents granted in respect of any such application (the "Patents") and all rights to claim priority from any of the same on the terms set out in this Agreement.

IT IS HEREBY AGREED

- 1 In consideration of the execution by the Assignee of the BPA the Assignor hereby assigns to the Assignee absolutely and with full title guarantee the Patents and the full and exclusive benefit thereof together with the right to recover and to take all such proceedings as may be necessary for the recovery of damages or otherwise in respect of all infringements of any of the Patents whether committed before or after the date of this Agreement.
- 2 The Assignor hereby covenants with the Assignee that the Assignor will at the expense of the Assignee execute all such documents and do any things that the Assignee may reasonably require to enable the Assignee or its nominee to enjoy the full benefit of the rights hereby assigned.

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REEL: 011792 FRAME: 0764

- 3 The Assignor warrants that so far as it is aware:
- 3.1 the Patents are free and clear of any licence, security interest, right or benefit to or in favour of any person;
- 3.2 none of the Patents are being infringed, revoked, objected to or opposed by any person;
- 3.3 the exercise by the Assignee of the rights granted by those Assignments will not infringe any rights of any third party.
- 4 This Agreement shall be governed by and interpreted in accordance with English law and the parties hereby submit the exclusive jurisdiction of the Courts of England and Wales.

### SCHEDULE

All Intellectual Property including the following and all equivalents, CIPs and divisionals, national application and all supporting documentation, information and laboratory notebooks.

REF No. CYCLACEL	DESCRIPTION	REF No. FLUORESCIENCE	PCT	US
1	Coiled-coil binding assays	WO99/11774	PCT GB98/02565	US 09/146,549
2	Protease assays	P005931	PCT GB00/00601	US 09/259,474
3	Immobilised assay formats	P005932	PCT GB00/00669	US 09/259,658
4	Natural domains - phos.	P006404	PCT GB00/00666	US 09/258,981
5	Natural domains - non-phos.	P006403 Combined in EU with P006404	n/a	US 09/259,478
6	Simultaneous assay	P008184	PCT GB00/00663	n/a
7	Fluorescent labelling		n/a	US 4256/85181
8	Protein DNA	P009006 GB	n/a	US 10069/1100
9	Confirmational state of protein	P006344GB	PCT GB00/00668	US 09/258,452
10	Modification of engineered binding partners	P006405GB	PCT GB00/0674	US 09/259,159
11	Transgenic mouse	P007360 GB	n/a (GB priority application)	n/a

Executed by the parties on the date set out above:

Signed by

for and on behalf of  
**Fluorescence Limited**

In the presence of:


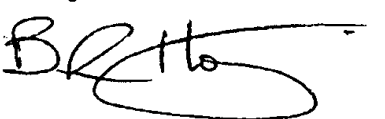
*[Signature]*  
*Katy Hudson L*  
2 STABLE COTTAGE, ALEXTON, DAKHMAN  
MARKETING EXEC. PATENT  
REEL: 011792 FRAME: 0765

Signed by

for and on behalf of  
Cyclacel Limited

In the presence of:

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RECORDED: 05/09/2001

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